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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,342	05/26/2000	YUKIO KATO	046124-5025	3974

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EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	15

DATE MAILED: 01/06/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/555,342	Applicant(s) KATO ET AL.	
	Examiner MINH-TAM DAVIS	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-13,15-17,19-21 and 25-38* is/are pending in the application.

4a) Of the above claim(s) *11-13,19-21,33 and 35-38* is/are withdrawn from consideration.

5)☒ Claim(s) *25* is/are allowed.

6)☒ Claim(s) *15-17,26-28,32 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Effective February 7, 1998, the Group Art Unit location has been changed, and the examiner of the application has been changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Minh-Tam Davis, Group Art Unit 1642.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicant cancels claim 14 and adds new claims 33-38 which are related to claims 15-17, 25-28 and 32.

Applicant's election with traverse of species SEQ ID Nos: 21 and 22, claim 34 in paper No:14 is acknowledged. The traverse is on the ground that it would not be serious undue experimentation to search all the primers, and that it would be unreasonable to require Applicants to file five divisional applications in order to cover these other claims. This is not found persuasive because the searches for all the primers are not-coextensive for reasons set forth in previous Office action, and it would be serious undue experimentation to search all the primers. Further, filing of five divisional applications in order to cover these other claims drawn to other primers is not required, because these are species.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 15-17, 25-28, 32 and 34, primers of SEQ ID Nos: 21 and 22 are examined in the instant application.

Claim 25 seems to be free of prior art and is allowable.

The following are the remaining rejections.

INFORMATION DISCLOSURE STATEMENT

The reference by Doolittle et al has been examined, and a new PTO-1449 has been issued, and supersedes the prior PTO-1449 of the Office action of paper No:9.

PRIORITY DATE

The Examiner has established a priority date May 26, 2000 for claim 34 of the instantly claimed application serial number 09/555342 as the application PCT/JP98/05348 to which priority is claimed does not recite the limitation of SEQ ID Nos: 21 and 22. Applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, NEW MATTER, NEW REJECTION

Claim 34 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 34 is drawn to an isolated nucleic acid molecule obtained by PCR amplification using primers having the sequences of SEQ ID Nos: 21 and 22.

It is noted that this application of SN= 09/555342 is not a CIP of PCT/JP98/05348, but is a 371 of PCT/JP98/05348, which is supposed to be identical to the parent case PCT/JP98/05348. However, although the present application of SN= 09/555342 discloses SEQ ID Nos: 21 and 22 and their use in PCR (page 30), the parent PCT/JP98/05348 does not disclose nor contemplate SEQ ID Nos: 21 and 22 and their use in PCR.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 16-17, 27-28, 32 are rejected under 112, first paragraph, pertaining to lack of a clear description of a nucleic acid encoding a protein that has 85% homology with fragments of SEQ ID NO:2, or a nucleic acid that hybridizes under stringent conditions to fragments of SEQ ID NO:1, or a complement of SEQ ID NO:1 or of a nucleic acid that is complementary to a nucleic acid encoding a fragment of at least 30 amino acids of SEQ ID NO:2, for the same reasons already of record in paper No: 9. It is noted that by typographic error, claim 26 was inadvertently not recited in the previous Office action, but it is clear that claim 26 would be included in the rejection.

Applicant argues that claims 27-28 are directed to sequences that are complementarly to at least 180 base pairs of SEQ ID NO:2 (probably Applicant meant SEQ ID NO:1, because SEQ ID NO:2 is a protein and not a nucleic acid sequence). Such sequences or fragments encoding at least 90 amino acids of SEQ ID NO:2 are clearly supported by the specification.

Applicant further asserts that claim 17 has been amended to clarify that stringent conditions allow hybridization of nucleic acids having 80% or more homology to a nucleic acid sequence ranging from the 49th to 3,183th bases in SEQ ID NO:1, which would include a defined genus of nucleic acids that is clearly distinguishable by those of skill in the art. Applicant asserts that claim 17 also requires that such a nucleic acid encodes a protein specifically expressed in differentiated chondrocytes versus dedifferentiated chondrocytes, which is clearly a functional attribute.

Applicant asserts that likewise, claim 16 requires that the encompassed nucleic acids be specifically expressed in differentiated chondrocytes versus dedifferentiated chondrocytes. Applicant asserts that claim 16 further defines which domains are subject to high homology (85%) limitation. Applicant asserts that the specification also discusses conservative substitution in protein variants.

Applicant asserts that claim 32 is dependent on all other claims and therefore, incorporates all the limitations thereof in each context.

Applicant's arguments in paper No: 10 have been considered but are not found to be persuasive for the following reasons:

It is noted that a complement could be a partial or full complement, wherein a partial complement could share with SEQ ID NO:1 or fragments of at least 180 base pair of SEQ ID NO:1 only a few nucleotides. Thus the claimed complementary sequences could share with SEQ ID NO:1 or its fragments only a few nucleotides.

It is also noted that a nucleic acid sequence comprising a fragment of at least 180 base pairs of SEQ ID NO:1 encompasses any nucleic acid sequence of any length

and any structure, provided said nucleic acid sequence shares a fragment of at least 180 base pairs with SEQ ID NO:1. For example, the claimed nucleic acid sequence would encompass an unrelated nucleic acid sequence taught by Rosen et al, Genbank Sequence Database (Accession AAB54227), National Center for Biotechnology Information, National Library of Medicine, Bethesda, Maryland, publicly available on 2000, which encodes a protein which is 97% similar to the claimed SEQ ID NO:2, from amino acid 565 to amino acid 907, as shown in MPSRCH sequence similarity search (MPSRCH search report, 2002, us-09-555-342-2.rag. page 4).

It is further noted that nucleic acids that hybridize to SEQ ID NO:1 under stringent conditions, wherein said stringent conditions allow hybridization of nucleic acids having 80% or more homology to a nucleic acid sequence ranging from the 49th to 3,183th bases in SEQ ID NO:1, encompass variants of SEQ ID NO:1 which have 80% sequence identity with SEQ ID NO:1.

The structure and the function of the claimed nucleic acids encoding protein variants of SEQ ID NO:2 or peptide variants of domains or fragments of SEQ ID NO:2 however are not disclosed in the specification. There is no disclosure of common attributes or characteristics that identify the members of the claimed nucleic acids encoding said protein or peptide variants. The specification and the claims do not place any limit on which amino acids to be subjected to conservative or non-conservative substitution, or deletion or addition, the type of substitution besides conservative substitution, nor the type of amino acids replacing the original amino acids. The specification and the claims do not place any limit on the number of amino acids that

could be substituted, deleted or added, provided that the upper limit of the variation is 15% or 20%.

Further, expression in differentiated chondrocytes versus dedifferentiated chondrocytes is not a specific function of a protein, because said expression could be shared by several other proteins that are specific for differentiated chondrocytes. Further, no common attributes that identify the claimed nucleic acid sequences encoding said protein or peptide variants are disclosed in the claims, because the function of a nucleic acid sequence could be abolished, even with substitution of a single amino acid of the proteins or peptides encoded by said nucleic acid sequences (Burgess et al, of record).

Thus Applicant is not in possession of the claimed nucleic acids encoding protein variants of SEQ ID NO:2 or peptide variants of the domains of SEQ ID NO:2.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE

1. Claim 16 is rejected under 112, first paragraph, pertaining to lack of enablement for a nucleic acid encoding a protein or peptide variant of SEQ ID NO:2 for the same reasons already of record in paper No: 9. The amended claim 17 is rejected for the same reason already of record in paper No:9.

Applicant argues that the method used for replacing, deleting or inserting particular amino acid residues is well known in the art. Applicant further asserts that the specification provides a list of conservative amino acid substitutions that are frequently tolerated in proteins and also define the domains most important for the function of

CDEP. Applicant asserts that one could easily select appropriate mutant protein having functions comparable to CDEP, using the assay taught by Koyano et al.

The recitation of the reference by Koyano et al is acknowledged.

Applicant's arguments in paper No: 10 have been considered but are not found to be persuasive for the following reasons:

It is noted that the amended claim 17, now drawn to nucleic acids that hybridize to SEQ ID NO:1 under stringent conditions, wherein said stringent conditions allow hybridization of nucleic acids having 80% or more homology to a nucleic acid sequence ranging from the 49th to 3,183th bases in SEQ ID NO:1, encompasses variants of SEQ ID NO:1 which have 80% sequence identity with SEQ ID NO:1.

It is further noted that the function of the claimed encoded variants are not recited in the claims. Thus the claims encompass numerous nucleic acids encoding variants of SEQ ID NO:2 with unknown function. Therefore, although the method used for replacing, deleting or inserting particular amino acid residues is well known in the art, without a known function, one would not know how to screen for the claimed nucleic acid sequences.

2. Claims 27-28 and 32 are rejected under 112, first paragraph, pertaining to lack of enablement for a nucleic acid that is complementary to SEQ ID NO:1 or fragments thereof, for the same reasons already of record in paper No: 9.

Applicant argues that the claims do not encompass any nucleotide sequence having variation from the claimed complementary sequence.

Applicant's arguments in paper No: 10 have been considered but are not found to be persuasive for the following reasons:

It is noted that a complement could be a partial or full complement, wherein a partial complement could share with SEQ ID NO:1 or fragments of at least 180 base pair of SEQ ID NO:1 only a few nucleotides. Thus the claimed complementary sequences could share with SEQ ID NO:1 or its fragments only a few nucleotides.

REJECTION UNDER 35 USC 112, FIRST PARAGRAPH, SCOPE, NEW REJECTION

Claims 17, 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:1, does not reasonably provide enablement for a gene comprising a DNA fragment of SEQ ID NO:1, or a DNA which hybridizes under stringent conditions to a fragment of SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 17, 32 are drawn to an isolated gene comprising a nucleic acid sequence ranging from the 49th to 3,183th bases in SEQ ID NO:1, or comprising a DNA which hybridizes under stringent conditions to a nucleic acid sequence ranging from the 49th to 3,183th bases in SEQ ID NO:1.

Claims17, 32 encompass a gene or a genomic DNA sequence comprising a nucleic acid sequence ranging from the 49th to 3,183th bases in SEQ ID NO:1, or a

DNA which hybridizes under stringent conditions to a nucleic acid sequence ranging from the 49th to 3,183th bases in SEQ ID NO:1.

The specification discloses isolation of a CDEP clone, i.e. a cDNA, that is expressed in chondrocytes but not in dedifferentiated chondrocytes, by substractive hybridization (p.26, first paragraph). No disclosure of a gene or a genomic DNA sequence comprising a DNA fragment of SEQ ID NO:1, or a DNA which hybridizes under stringent conditions to a fragment of SEQ ID NO:1.

One cannot extrapolate the teaching in the specification to the claims for the following reasons: The specification fails to identify and describe the 5' and 3' regulatory regions and untranslated regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the gene. The art indicates that the structures of genes with naturally occurring regulatory elements and untranslated regions is empirically determined (Harris et al. J. of The Am Society of Nephrology 6:1125-33, 1995; Ahn et al. Nature Genetics 3(4):283-91, 1993; and Cawthon et al. Genomics 9(3):446-60, 1991). Therefore, the structure of these elements is not conventional in the art.

In view of the above, it would have been undue experimentation for one of skill in the art to practice the claimed invention.

REJECTION UNDER 35 USC 102, NEW REJECTION

Claim 34 is rejected under 35 U.S.C. 102(b) as being anticipated by Koyano, Y et al, 1997, of record.

Claim 34 is drawn to an isolated nucleic acid molecule obtained by PCR amplification using primers having the sequences of SEQ ID Nos: 21 and 22.

Using primers of SEQ ID Nos: 21 and 22, the claimed nucleic acid sequence would comprise nucleotide 1733 to nucleotide 2501 of SEQ ID NO:1, since SEQ ID NO:21 consists of nucleotide 1733 to 1372, and SEQ ID NO:22 consists of nucleotide 2482 to nucleotide 2501.

Koyano, Y et al teach a sequence which encompasses nucleotides 1733 to 2501 of the claimed SEQ ID NO:1, as shown by MPSRCH sequence similarity search (MPSRCH sequence similarity search report, 2002, us-09-555-342b-1-copy-1733-2501.rge, pages 1-2).

Given the polynucleotide sequence taught by Koyano, Y et al, one of ordinary skill in the art would immediately envision the claimed polynucleotide.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 703-305-2008. The examiner can normally be reached on 9:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, ANTHONY CAPUTA can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0916.

SUSAN UNGAR, PH.D
PRIMARY EXAMINER

MINH TAM DAVIS

December 13, 2002